

**Summary of discussions at IRIS Board meeting in Seattle (5-24-00) and St Aubin (9-13-00) regarding treatment of Stages I to IV chronic renal insufficiency/failure patients; modified at Barcelona (9-7-04)**

All treatments for chronic renal disease (CRD) need to be tailored to the individual patient. The following recommendations are useful starting points for the majority of animal at each stage. Serial monitoring of these patients is ideal and treatment should adapted accordinging to the response to treatment.

**Stage 1 Canine patients:**

Discontinue all potentially nephrotoxic drugs

Identify and treat any prerenal or post-renal abnormalities

Rule out any treatable conditions like pyelonephritis (any urinary tract infection (UTI) should be regarded as a potential pyelonephritis and treated appropriately) and renal urolithiasis with radiographs and/or ultrasonography

Measure blood pressure

*Management of dehydration:*

These patients have decreased urine concentrating ability and therefore

- 1) correct clinical dehydration/hypovolemia with isotonic, polyionic fluid solutions (e.g., lactated ringers and Normosol R) IV or SQ as needed
- 2) have fresh water available at all times for drinking

*Systemic hypertension:*

The blood pressure needed to prevent renal disease progression is unknown - our goal is to reduce blood pressure (to a systolic pressure < 160 mm Hg) and minimize risk extra-renal end organ damage (CNS, retinal, cardiac problems/damage). If there is no evidence of extra-renal end organ damage but the blood pressure persistently exceeds 160 mm Hg, increasing the risk of extra-renal end organ damage, treatment should be instituted. 'Persistence' of the elevation should be judged on multiple BP measurements made over 2 months (if at mild to moderate risk – 160 to 179 mm Hg systolic BP) or over 1 to 2 weeks (if at severe risk -  $\geq 180$  mmHg). If evidence of end organ damage exists, animals should be treated without the need to demonstrate persistence of elevated blood pressure. Reducing blood pressure is a long term aim managing the patient with CKD and a gradual and sustained reduction in blood pressure should be the goal avoiding any sudden or severe decreases leading to hypotension. A logical stepwise approach to managing hypertension is as follows:

- 1) dietary Na reduction - there is no evidence that lowering dietary Na is beneficial. If dietary Na reduction is attempted, it should be accomplished gradually.
- 2) Angiotensin converting enzyme inhibitor (ACEI) therapy standard dose rate
- 3) Double the dose of ACEI (in some patients, increasing the dose may improve the antihypertensive effect)
- 4) Combination ACEI and Calcium channel blocker (CCB; e.g. amlodipine) treatment
- 5) Combine ACEI, CCB (e.g. amlodipine) and hydralazine treatment

*Monitoring response to antihypertensive treatment:*

Hypertensive animals normally require life-long therapy and may require adjustments – serial monitoring is essential. After stabilization monitoring should occur at least every 3 months

SBP <120 mmHg and/or clinical signs (weakness, tachycardia) indicates hypotension which is to be avoided)

Plasma creatinine -reducing blood pressure may lead to small and persistent increases in plasma creatinine (<0.5 mg/dl or 50 umol/l increase) concentration, but a marked increase suggests an adverse drug effect while progressively increasing plasma creatinine indicates progressive kidney damage/disease.

*Proteinuria:*

For dogs in stage 1, those with urine protein to creatinine ratio (UP/C) > 2.0 should be investigated for disease processes leading to proteinuria (see 1 and 2 below) and treated with anti-proteinuric drugs (see 3 below). Dogs in stage 1 with less marked proteinuria (UP/C >1.0 but >2.0) may require thorough investigation (see 1 and 2 below) and close monitoring (see 5 below) and those with mild proteinuria (>0.5 but <1.0) require close monitoring (see 5 below)

- 1) look for any concurrent associated disease process that may be treated/corrected
- 2) Consider kidney biopsy as a means of identifying underlying disease (consult experts if unsure of indications for kidney biopsy);
- 3) ACEI with dietary protein reduction
- 4) low-dose aspirin (0.05-0.5 mg/kg/day) if serum albumin is < 2.0 g/dl
- 5) Monitor response to treatment / progression of disease  
Stable plasma creatinine concentration and decreasing UPC – good response  
Serially increasing plasma creatinine concentration and/or increasing UPC – disease is progressing

Note: ACEI use is contraindicated in any animal that is clinically dehydrated and/or is showing signs of hypovolaemia. Correct dehydration before using of these drugs otherwise glomerular filtration rate (GFR) may drop precipitously.

**Stage 2 Canine patients:**

All of the above listed for stage 1 plus:

The intervention point for treatment of proteinuria should be reduced to UPC of 0.5 in dogs that are azotaemic

*If metabolic acidosis exists (blood bicarbonate or total CO<sub>2</sub> < 18 mmol/l) once the patient is stabilized on the diet of choice:*

Supplement with oral sodium bicarbonate or potassium citrate to effect to maintain blood HCO<sub>3</sub>/TCO<sub>2</sub> in the range of 18-24 mmol/l.

*Reduction of phosphate intake:*

Evidence suggests that chronic reduction of phosphate intake to maintain a plasma phosphate concentration below 1.5 mmol/l (not less than 0.9 mmol/l) (<4.6 mg/dl but >2.7 mg/dl) is beneficial to patients with CKD. The following measures can be introduced sequentially in an attempt to achieve this:

- 1) dietary phosphorus restriction
- 2) if plasma phosphate concentration remains above 1.5 mmol/l (4.6 mg/dl) after dietary restriction, give enteric phosphate binders (e.g., aluminium hydroxide, aluminium carbonate, calcium carbonate, calcium acetate) to effect (starting at 30-60 mg/kg with each feeding – mixed with the food if possible). The dose required will vary according to the amount of phosphate being fed and the stage of kidney disease. Treatment with phosphate binders should be to effect (as outlined above) with signs of toxicity limiting the upper dose rate possible in a given patient. Monitor serum calcium and phosphate concentrations every 4-6 weeks until stable and then every 12 weeks. Microcytosis and or generalized muscle weakness suggests aluminium toxicity if using an aluminium containing binder – switch to another form of phosphate binder should this occur. Hypercalcaemia should be avoided – combinations of aluminium and calcium containing phosphate binders may be necessary in some cases.

Note: ACEI use is contraindicated in any animal that is clinically dehydrated and/or is showing signs of hypovolaemia. Correct dehydration before using of these drugs otherwise glomerular filtration rate (GFR) may drop precipitously.

**Stage 3 canine patients:**

All of the above listed for stage 1 and 2 patients plus:

If plasma phosphate exceeds 1.5 mmol/l after maximal palatable phosphate binder dose has been achieved and hyperparathyroidism is documented (i.e., increased blood PTH concentration) consider use of ultra-low dose calcitriol (such use is controversial and requires careful monitoring of blood phosphate, PTH, and ionized calcium concentrations).

Additional recommendations for stage 3 patients:

- 1) appropriate dietary protein reduction in order to decrease blood urea and phosphate concentrations
- 2) consider treatment for anemia if it is affecting the patient's quality of life (typically this occurs when the PCV is  $\leq 0.20$  l/l) Human recombinant erythropoietin is the most effect treatment but it is not approved for veterinary use. Anabolic steroids are of not proven benefit and may be detrimental.
- 3) treat vomiting/decreased appetite/nausea with H2 receptor blockers (e.g., ranitidine) and antiemetics (e.g., metoclopramide).
- 4) give fluids parenterally as necessary to maintain hydration

Note: ACEI use is contraindicated in any animal that is clinically dehydrated and/or is showing signs of hypovolaemia. Correct dehydration before using of these drugs otherwise glomerular filtration rate (GFR) may drop precipitously.

Drugs that rely predominantly on renal function for their clearance from the body should be used with caution in patients in stage 3 CKD and above. It may be necessary to adjust the dose of these drugs (depending on their therapeutic indices) to avoid accumulation.

**Stage 4 canine patients:**

All of the above listed for stages 1 to 3 patients plus:

Intensify efforts to prevent protein/calorie malnutrition. One may need to consider feeding tube intervention (e.g., percutaneous gastrostomy tube).

Intensify efforts to prevent dehydration. Feeding tubes can be used administer fluids as well as food.

Consider dialysis and/or renal transplantation.

In treating based on proteinuria or BP – use recommendations under stage 3; NB take care not to introduce ACE inhibitor treatment to unstable dehydrated animals where GFR may drop precipitously if ACE inhibitors are introduced before the patient is adequately hydrated

## Treatment recommendations for cats with CRF

Recommendations are similar to those proposed for dogs with the following exceptions:

### Stage 1 – Feline Patients

#### *Systemic hypertension*

The blood pressure needed to prevent renal disease progression is unknown - our goal is to reduce blood pressure to a systolic pressure < 160 mm Hg and to minimize the risk of extra-renal end organ damage (CNS, retinal, cardiac problems/damage). If there is no evidence of extra-renal end organ damage but systolic blood pressure persistently exceeds 160 mmHg risking extra-renal end organ damage, treatment should be instituted. 'Persistence' of the elevation should be judged on multiple BP measurements made over 2 months (if at mild to moderate risk – 160 to 179 mm Hg systolic BP) or over 1 to 2 weeks (if at severe risk -  $\geq 180$  mmHg). If evidence of end organ damage exists, animals should be treated without the need to demonstrate persistence of elevated blood pressure. If hypertensive feline patients are proteinuric, this also needs to be treated in addition to the hypertension. Reducing blood pressure is a long term aim managing the patient with CKD and a gradual and sustained reduction in blood pressure should be the goal avoiding any sudden or severe decreases leading to hypotension. A logical stepwise approach to managing hypertension is as follows:

- 1) dietary Na reduction - there is no evidence that lowering dietary Na is beneficial. If dietary Na reduction is attempted, it should be accomplished gradually.
- 2) CCB - (e.g. amlodipine)
- 3) Increase the dose of amlodipine up to 0.5 mg/kg daily
- 4) Combination ACEI and CCB treatment

#### *Monitoring response to antihypertensive treatment:*

Hypertensive animals normally require life-long therapy and may require repeated adjustments – serial monitoring is essential. Frequency of monitoring after stabilization should be at least every 3 months SBP < 120 mmHg and/or clinical signs (weakness, tachycardia) indicates hypotension which is to be avoided)

Plasma creatinine (reducing blood pressure may lead to small and persistent increases in plasma creatinine concentration (<0.5 mg/dl or 50  $\mu$ mol/l increase), but marked increases in plasma creatinine suggest an adverse drug effect while progressively increasing plasma creatinine indicates progressive kidney damage/disease)

### Stage 2 – Feline Patients

Metabolic acidosis has to be considered when blood bicarbonate or total CO<sub>2</sub> < 16 mmol/l

Hyperphosphatemia : many cats in stage 2 will have normal plasma phosphate concentrations but will have increased plasma PTH concentration

If the patient is hypokalemic, then potassium gluconate should be supplemented to effect (typically 1-2 mmol/kg/day).

### Treatment of proteinuria (all stage) – Feline Patients

The intervention points recommended for treating proteinuria in the cat differ from the dog when the feline patient is azotaemic. The intervention points for the feline patient are:

- Non-azotaemic cats (Stage 1 and early stage 2) – UPC intervention point >2.0 [as for dogs]
- Azotaemic cats (Stage 2 and above) – UPC intervention point >0.4

The same warnings about the introduction of ACEI to animals that are dehydrated and hypovolaemic apply.

The same cautions about the use of drugs that rely on the kidneys for their clearance and their use in patients with stage 3 and 4 CKD apply to cats